REMARKS

Entry of this preliminary amendment prior to examination is respectfully requested. After entry of the preliminary amendment, claims 1-6, 8-11, 13, 14 and 17-22 are pending.

The specification is amended at page 13, line 12 to replace a clerical error in the recited species. Support for this amendment is found in the application as filed, at page 42, lines 3-11, which correctly identify compound 3a as "1-(2-6-chloro-1H-indol-3-yl)-4-(1H-indol-4-yl) piperidine."

The specification is also amended at page 28, lines 21-27, to correct the title of the paragraph, to recite "5-fluorobenzofuran-3-yl acetic acid." Support for this amendment is found at page 29, lines 24-25.

The specification is further amended at page 31, line 20, to correct an obvious clerical error.

Claim 1 is amended to limit the claims to the subject matter restricted out of parent application serial no. 09/719,849, to recite that W is C, CH or COH. Claim 13 is amended to delete the species not covered in this application. Claims 7 and 12, which did not cover the restricted subject matter, are canceled.

Non-statutory "use" claims 15 and 16 are canceled.

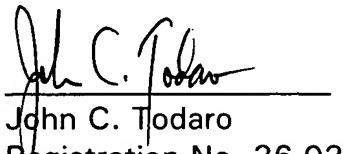
Claim 1 is also amended to improve clarity by deleting the expression "and/or," and replace same with "or." This amendment does not change the scope

of the claim. Claims 6, 11, 14, 17 and 18 are amended to remove multiple dependencies, and to clarify the language of the claims.

An early and favorable examination is earnestly solicited.

Dated: January 15, 2002

Respectfully submitted,



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File No.: 5432/1H967US1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of: Date: January 15, 2002

MOLTZEN, et al.

Serial No: To be assigned (Divisional Application of U.S. Patent Application Serial No. 09/719,849, Filed February 2, 2001)

Filed: Concurrently herewith

For: 4,5,6 AND 7-INDOLES AND INDOLINE DERIVATIVES, THEIR PREPARATION AND USE

MARKUP TO PRELIMINARY AMENDMENT UNDER 37 C.F.R. §1.121

Hon. Commissioner of
Patents and Trademarks
Washington, DC 20231

Sir:

IN THE SPECIFICATION

Page 13, line 12:

1-(2-(6-Chloro-1H, indol-3-yl)ethyl-4-(1H-indol-4-yl)piperidine;

Page 28, line 21:

C. Preparation of 5-fluorobenzofuran-3-yl acetic acid.

Please replace the fourth full paragraph, page 31, lines 15-20 with the following:

1d, *1-(4-(5-Fluoro-3-benzofuranyl)-1-butyl)-4-(1H-indol-4-yl)piperazine, dihydrochloride.*

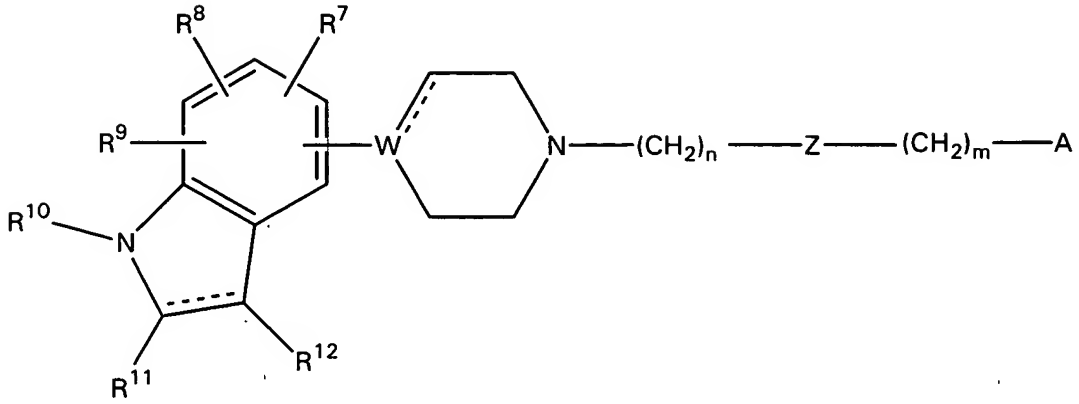
Mp 241-44°C, ^{1}H NMR (DMSO-d_6): 1.65-1.95 (m, 4H); 2.70 (t, 2H); 3.15-3.40 (m, 6H); 3.60 (d, 2H); 3.70 (d, 2H); 6.50 (s, 1H); 6.55 (d, 1H); 7.00 (t, 1H); 7.10 (d, 1H); 7.15 (dt, 1H); 7.30 (t, 1H); 7.45-7.60 (m, 2H); 7.90 (s, 1H); 10.95 (b, 1H); 11.20 (s, 1H). MS m/z (%): 392 ([MH?]MH+, 90%), 234 (19%), 199 (23%), 163 (49%), 131 (11%).

IN THE CLAIMS

Please amend claims 1, 6, 11, 13, 14, 17 and 18 as follows.

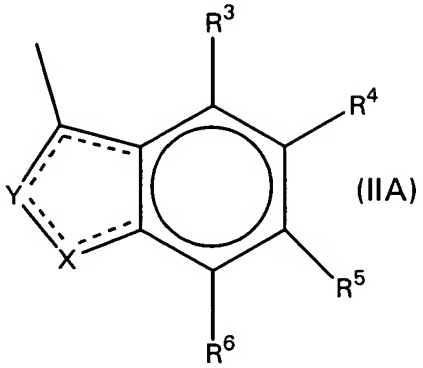
1. (Amended) A substituted 4-, 5-, 6-, or 7-indole or indoline derivative of Formula

wherein W is [N,] C, CH or COH and the dotted lines indicate optional bonds and



(I)

wherein A is a group having the formula



(IIA)

wherein X is CR^{1A}, CHR^{1A}, N, NR^{1B}, O, or S, where R^{1A} is as defined for R^3 to R^9 below, and where R^{1B} is as defined for R^{10} below;

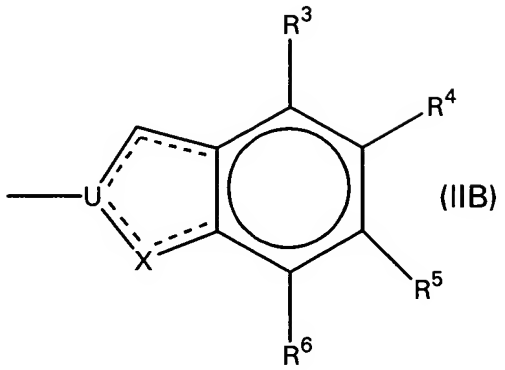
Y is CR^{2A}, CHR^{2A}, N, NR^{2B}, O, or S, where R^{2A} is as defined for R^3 to R^9 below

and where R^{2B} is as defined for R^{10} below, and

the dotted lines indicate optional bonds;

provided that X and Y are not both O or S;

A is a group having the formula



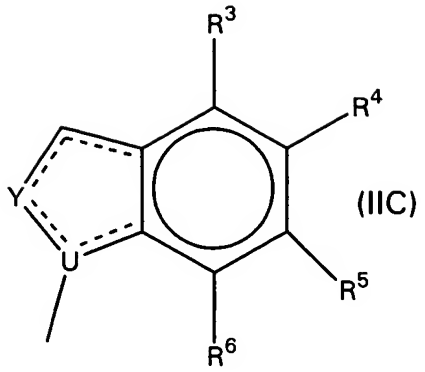
(IIB)

wherein X is CR^{1A}, CHR^{1A}, N, NR^{1B}, O, or S, where R^{1A} is as defined for R^3 to R^9 below, and where R^{1B} is as defined for R^{10} below;

U is C, CH, or N; and

the dotted lines indicate optional bonds; or

A is a group having the formula



(IIC)

wherein U is C, CH, or N;

Y is CR^{2A}, CHR^{2A}, N, NR^{2B}, O, or S, where R^{2A} is as defined for R^3 to R^9 below and where R^{2B} is as defined for R^{10} below; and

the dotted lines indicate optional bonds;

n is 0, 1, 2, 3, 4, or 5, and m is 0, 1, 2, 3, 4, or 5;

Z is CH_2, O, S, CO, SO, or SO_2, provided that if n is 0 then Z is CH_2;

R^3-R^9 and R^{11} to R^{12} are independently selected from hydrogen, halogen, cyano, nitro, C_{1-6}-alk(en/yn)yl, C_{1-6} alkoxy, C_{1-6} alkylthio, hydroxy, hydroxy-C_{1-6}-alkyl, C_{1-6} alkoxycarbonyl, C_{3-8} cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, C_{1-6} alkylcarbonyl, phenylcarbonyl, halogen substituted phenylcarbonyl, trifluoromethyl,

trifluoromethylsulfonyloxy, C_{1-6} alkylsulfonyl, aryl and heteroaryl, [and/or] or two adjacent groups taken from R^3 - R^9 may together form a methylenedioxy group, [and/or] or two adjacent groups R^7 - R^9 may together form a cyclopentyl or cyclohexyl ring which may be substituted with one or more methyl groups, [and/or] or one of R^3-R^9 may alternatively be a group $-NR^{13}R^{14}$ wherein R^{13} is as defined for R^{10} below and R^{14} is hydrogen, C_{1-6} alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6} alk(en/yn)yl, aryl, heteroaryl, aryl-C_{1-6} alkyl, or heteroaryl-C_{1-6}-alkyl;

R^{10} is

- hydrogen, C_{1-6} alk(en/yn)yl, C_{3-8}-cycloalk(en)yl, C_{3-8} cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, aryl, heteroaryl, aryl-C_{1-6} alkyl, heteroaryl-C_{1-6}- alkyl, acyl, thioacyl, C_{1-6}-alkylsulfonyl, trifluoromethylsulfonyl; arylsulfonyl, or heteroarylsulfonyl;
- $R^{15}VCO$- wherein V is O or S and R^{15} is C_{1-6}-alk(en/yn)yl, C_{3-8} cycloalk(en)yl, C_{3-8}-cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, aryl, or heteroaryl; or
- a group $R^{16}R^{17}NCO$- or $R^{16}R^{17}NCS$- wherein R^{16} and R^{17} are independently selected from hydrogen, C_{1-6} alk(en/yn)yl, C_{3-8} cycloalk(en)yl, C_{3-8} cycloalk(en)yl-C_{1-6}-alk(en/yn)yl, heteroaryl, or aryl, or R^{16} and R^{17} together with the N-atom to which they are linked, form a pyrrolidinyl, piperidinyl, morpholinyl, or perhydroazepin group;

or an acid addition salt thereof.

6. (Amended) A compound according to [claims 1 to 5] claim 1 wherein Z is CH_2 and n + m is 0, 1, 2, 3, 4, 5, or 6.

11. (Amended) A compound of [claims 1-10] claim 1 wherein Z is CH_2 and n + m is 0, 1, 2, 3, 4, 5, or 6 and R^3-R^9 and R^{11}-R^{12} is hydrogen, halogen, cyano, nitro, C_{1-6}-alkyl, C_{1-6}-alkoxy, hydroxy, hydroxy-C_{1-6}-alkyl, C_{1-6}-alkoxycarbonyl and trifluoromethyl; and R^{10} is hydrogen.

13. (Amended) A compound according to claim 1 which is

[1-(2-(3-Benzofuranyl)ethyl)-4-(1H-indol-4-yl)piperazine,

1-(3-Benzofuranylmethyl)-4-(1H-indol-4-yl)piperazine,

1-(2-(5-Fluoro-3-benzofuranyl)ethyl)-4-(1H-indol-4-yl)piperazine,

1-(4-(5-Fluoro-3-benzofuranyl)-1-butyl)-4-(1H-indol-4-yl)piperazine,

1-(2-(1H-Indol-3-yl)ethyl)-4-(1H-indol-4-yl)piperazine,

1-(3-(1H-Indol-3-yl)-1-propyl)-4-(1H-indol-4-yl)piperazine,

1-(4-(1H-Indol-3-yl)-1-butyl)-4-(1H-indol-4-yl)piperazine,

1-(3-(5-Fluoro-3-benzofuranyl)-1-propyl)-4-(1H-indol-4-yl)piperazine,

1-(2-(2-Methyl-4,5,6,7-tetrafluoro-3-benzofuranyl)ethyl)-4-(1H-indol-4-yl)piperazine,

1-(2-(3-Indazolyl)ethyl)-4-(1H-indol-4-yl)piperazine,

1-(2-(6-Chloro-3-indazolyl)ethyl)-4-(1H-indol-4-yl)piperazine,

1-(2-(7-Cyano-1H-indol-3-yl)ethyl)-4-(1H-indol-4-yl)piperazine,

1-(2-(6-Chloro-1H-indol-3-yl)ethyl)-4-(1H-indol-4-yl)piperazine,

1-(2-(4-Chloro-1H-indol-3-yl)ethyl)-4-(1H-indol-4-yl)piperazine,

1-(2-(5-Fluoro-1H-indol-3-yl)ethyl)-4-(1H-indol-4-yl)piperazine,]

1-(2-(6-Chloro-1H-indol-3-yl)ethyl)-4-(1H-indol-4-yl)-1,2,3,6-tetrahydropyridine,

1-(2-(5-Fluoro-1H-indol-3-yl)ethyl)-4-(1H-indol-4-yl)-1,2,3,6-tetrahydropyridine, to

[1-(2-(7-Bromo-1H-indol-3-yl)ethyl)-4-(1H-indol-4-yl)piperazine,

1-(1-Allyl-1H-indol-4-yl)-4-(2-(6-chloro-1H-indol-3-yl)ethyl)piperazine,

1-(1-Allyl-1H-indol-4-yl)-4-(2-(5-fluoro-1H-indol-3-yl)ethyl)piperazine,

1-(1-Benzyl-1H-indol-4-yl)-4-(2-(6-chloro-1H-indol-3-yl)ethyl)piperazine,

1-(1-Benzyl-1H-indol-4-yl)-4-(2-(5-fluoro-1H-indol-3-yl)ethyl)piperazine,

1-(1-Benzyl-1H-indol-4-yl)-4-(2-(5-bromo-1H-indol-3-yl)ethyl)piperazine,

1-(2-(6-Chloro-1H-indol-3-yl)ethyl)-4-(1-propargyl-1H-indol-4-yl)piperazine,

1-(2-(1H-Indol-3-yl)ethyl)-4-(1-propargyl-1H-indol-4-yl)piperazine,

1-(2-(5-Fluoro-1H-indol-3-yl)ethyl)-4-(1-propargyl-1H-indol-4-yl)piperazine,

1-(2-(5-Bromo-1H-indol-3-yl)ethyl)-4-(1-propargyl-1H-indol-4-yl)piperazine,

1-(1-Benzyl-1H-indol-4-yl)-4-(2-(1H-indol-3-yl)ethyl)piperazine,

1-(2-(5-Bromo-1H-indol-3-yl)ethyl)-4-(1H-indol-5-yl)piperazine,

1-(2-(5-Chloro-1H-indol-3-yl)ethyl)-4-(1H-indol-5-yl)piperazine,

1-(2-(5-Fluoro-1H-indol-3-yl)ethyl)-4-(6-hydroxymethyl-1H-indol-4-yl)piperazine,

1-(2-(6-Chloro-1H-indol-3-yl)ethyl)-4-(6-hydroxymethyl-1H-indol-4-yl)piperazine,

1-(2-(5-Bromo-1H-indol-3-yl)ethyl)-4-(6-hydroxymethyl-1H-indol-4-yl)piperazine,

1-(3-(6-Fluoro-1,2-benzisoxazol-3-yl)-1-propyl)-4-(1H-indol-4-yl)piperazine,

1-(2-(1H-Indol-3-yl)ethyl)-4-(6-methoxycarbonyl-1H-indol-4-yl)piperazine,

1-(2-(6-Chloro-1H-indol-3-yl)ethyl)-4-(6-methoxycarbonyl-1H-indol-4-yl)piperazine,

1-(2-(5-Fluoro-3-benzofuranyl)ethyl)-4-(6-methoxycarbonyl-1H-indol-4-yl)piperazine,

1-(5-Fluoro-3-benzofuranylmethyl)-4-(1H-indol-4-yl)piperazine,

1-(3-Cyano-1H-indol-4-yl)-4-(2-(1H-indol-3-yl)ethyl)piperazine,

1-(3-Cyano-1H-indol-4-yl)-4-(2-(5-fluoro-3-benzofuranyl)ethyl)piperazine,

1-(2-(6-Chloro-1H-indol-3-yl)ethyl)-4-(3-cyano-1H-indol-4-yl)piperazine,

1-(2-(3-Benzofuranyl)ethyl)-4-(3-cyano-1H-indol-4-yl)piperazine,

1-(1H-Indol-4-yl)-4-(2-(5-methyl-3-benzofuranyl)ethyl)piperazine,

1-(1H-Indol-4-yl)-4-(2-(4-methyl-3-benzofuranyl)ethyl)piperazine,]

1-(3-(5-Fluoro-3-benzofuranyl)-1-propyl)-4-(1H-indol-4-yl)-1,2,3,6-tetrahydropyridine,

[1-(2-(5-Chloro-3-benzofuranyl)ethyl)-4-(1H-indol-4-yl)piperazine,

1-(1H-Indol-4-yl)-4-(2-(6-methyl-3-benzofuranyl)ethyl)piperazine,

1-(2-(7-Chloro-3-benzofuranyl)ethyl)-4-(1H-indol-4-yl)piperazine,

1-(2-(4-Chloro-1H-indol-3-yl)ethyl)-4-(3-cyano-1H-indol-4-yl)piperazine,]

1-(2-(6-Chloro-1H-indol-3-yl)-4-(1H-indol-4-yl)piperidine,

[1-(2-(5-Chloro-1H-indol-3-yl)ethyl)-4-(1H-indol-4-yl)piperazine,

1-(2-(7-Bromo-1H-indol-3-yl)ethyl)-4-(1H-indol-4-yl)piperazine,

1-(2-(4-Chloro-1H-indol-3-yl)ethyl)-4-(1H-indol-4-yl)piperazine,

1-(2-(6-Trifluoromethyl-1H-indol-3-yl)ethyl)-4-(1H-indol-4-yl)piperazine,

1-(1H-Indol-4-yl)-4-(2-(5-methyl-1H-indol-3-yl)ethyl)piperazine,

1-(1H-Indol-4-yl)-4-(2-(6-methyl-1H-indol-3-yl)ethyl)piperazine,

1-(1H-Indol-4-yl)-4-(2-(7-methyl-1H-indol-3-yl)ethyl)piperazine,

1-(2-(4,5-Dichloro-3-benzofuranyl)ethyl)-4-(1H-indol-4-yl)piperazine,

1-(2-(5-Bromo-3-benzofuranyl)ethyl)-4-(1H-indol-4-yl)piperazine,]

1-(2-(4-Chloro-1H-indol-3-yl)ethyl)-4-(1H-indol-4-yl)piperidine,

4-(1H-Indol-4-yl)-1-(2-(5-methyl-1H-indol-3-yl)ethyl)piperidine,

4-(1H-Indol-4-yl)-1-(2-(1H-indol-3-yl)ethyl)piperidine,

[1-(1H-Indol-4-yl)-4-(3-(4-methyl-3-benzofuranyl)-1-propyl)piperazine,]

4-(1H-Indol-4-yl)-1-(3-(4-methyl-3-benzofuranyl)-1-propyl)piperidine,

[1-(3-(4-Chloro-3-benzofuranyl)-1-propyl)-4-(1H-indol-4-yl)piperazine,

1-(2-(6-Chloro-1H-indol-3-yl)ethyl)-4-(6-chloro-1H-indol-4-yl)piperazine,

1-(2-(6-Chloro-1H-indol-3-yl)ethyl)-4-(6-fluoro-1H-indol-4-yl)piperazine,

1-(2-(6-Chloro-1H-indol-3-yl)ethyl)-4-(6-cyano-1H-indol-4-yl)piperazine,

1-(2-(6-Chloro-1H-indol-3-yl)ethyl)-4-(7-chloro-1H-indol-4-yl)piperazine,

1-(2-(6-Chloro-1H-indol-3-yl)ethyl)-4-(7-cyano-1H-indol-4-yl)piperazine,

1-(2-(6-Chloro-1H-indol-3-yl)ethyl)-4-(2-cyano-1H-indol-4-yl)piperazine,

1-(2-(6-Chloro-1H-indol-3-yl)ethyl)-4-(1H-indolin-4-yl)piperazine,

1-(2-(6-Chloro-1H-indol-3-yl)ethyl)-4-(1H-indol-6-yl)piperazine and

1-(2-(6-Chloro-1H-indol-3-yl)ethyl)-4-(1H-indol-7-yl)piperazine] or a pharmaceutically acceptable acid addition salt thereof.

14. (Amended) A pharmaceutical composition comprising a compound according to [claims 1 to 13] claim 1 or a pharmaceutically acceptable acid addition salt thereof and at least one pharmaceutically acceptable carrier or diluent.

17. (Amended) A method for the treatment of a disorder or disease of a living animal body, [including a human,] which is responsive to the inhibition of serotonin reuptake and antagonism of 5-HT_{1A} receptors comprising administering to such a living animal body, [including a human,] a therapeutically effective amount of a compound according to [claims 1 to 13] claim 1 or a pharmaceutically acceptable

acid addition salt thereof.

18. (Amended) A method for the treatment of an affective disorder[, including depression psychosis, anxiety disorders including general anxiety disorder and panic disorder and obsessive compulsive disorder] in a living animal body, [including a human,] comprising administering a therapeutically effective amount of a compound according to [claims 1 to 13] claim 1 or a pharmaceutically acceptable acid addition salt thereof.

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